REMARKS

In the Office Action of August 29, 2003, Claims 1 - 5 were rejected. No claim was allowed. In response, Claims 1 and 5 are amended, Claims 2 and 3 are canceled and new Claim 11 is added to the application. Reexamination and reconsideration are respectfully requested in view of the foregoing amendments and the following remarks.

Support for Amendments and New Claim and Request for Entry

Claims 1 and 5 and new Claim 11 are amended to be restricted to an embodiment that the Examiner has acknowledged is supported in the specification. In particular, Claim 1 is amended to limit the amino acid produced to L-histidine. New Claim 11 provides that the aminoquinoline eriviative is primaquine and the microorganism belongs to the genus *Escherichia*. Claim 5 is amended to provide that the microorganism is *E. coli* H-9341. Accordingly, it is respectfully submitted that the amendments presented herein do not raise new issues for consideration. Entry of the amendments and new claim is respectfully requested.

Rejection of Claim 5 under 35 U.S.C. §112, first paragraph

Claim 5 was rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that is not described in the specification. In particular, the Office Action alleges that no basis or support is found for the production and accumulation of all of the recited amino acids or for resistance of this organism to all of the aminoquinoline derivatives recited. The Office Action acknowledges that

resistance to primaquine by *E.coli* H-9341 and the production of amino acid histidine are shown.

In response, Claim 5 is amended to depend from new Claim 11, which depends from Claim 1. In Claim 11, the aminoquinoline derivative is limited to primaquine and the microorganism is limited to the genus *Escherichia*. In amended Claim 1, the amino acid produced is limited to L-histidine. Thus, Claim 5 is supported by the specification, for example on page 12, table 2.

Accordingly, it is respectfully submitted that the rejection of Claim 5 under 35 U.S.C. §112, first paragraph, is thereby overcome.

Rejection of Claims 1 - 5 under 35 U.S.C. §112, second paragraph

Claims 1 - 5 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner alleges that in Claim 1, it is unclear whether the limitation "having resistance to an aminoquinoline derivative ... at 150mg/l in a culture medium" means that this amount is provided every time the strain is cultured for the production of an amino acid.

In response, Claim 1 is amended to clarify that the method is a method for producing L-histidine by culturing a microorganism in a culture medium, and that the microorganism is defined by having a resistance to 150mg/l aminoquinoline derivative or its alkali metal salt.

Accordingly, it is respectfully submitted that all of the rejections of Claims 1 - 5 under 35 U.S.C. §112, second paragraph, are thereby overcome.

Rejection of Claims 1 - 4 under 35 U.S.C. §103(a) over Kino taken with

Stanbury

Claims 1 - 4 were rejected under 35 U.S.C. §103(a) as obvious over Kino et al (U.S. Patent No. 5,275,940) taken with Stanbury et al, "Principles of Fermentation Technology:, 1984, Pergamon Press, pp 43 - 47. The Examiner alleges that Kino teaches the production of an amino acid with a strain of *Corynebacterium glutamicum* that is resistant to an aminoquinoline derivative. The Examiner refers to the previous Office Action, in which it was alleged that a person skilled in the art would have expected any strain to produce and accumulate a variety of amino acids at least to some extent. The Examiner further alleges that Stanbury teaches that it is old to screen and select microorganisms for increased amino acid production by isolating mutants having amino acid analogue resistance. The Examiner concludes that it would have been obvious to modify the process of Kino by culturing the same or other microorganisms for the production of amino acids.

This rejection is respectfully traversed as it may be applied to Claims 1 and 4 - 5 as amended herein and to new Claim 11. In particular, independent Claim 1 is amended to provide that the amino acid produced is L-histidine. Kino et al. disclose overproduction of tryptophan by using a microorganism belonging to the genus *Corynebacterium* or *Brevibacterium*, wherein the microorganism has resistance to aminoquinoline derivative. However, they are silent about producing L-histidine by a microorganism recited in Claim 1.

As is well known, the biosynthesis pathway for L-tryptophan and the biosynthesis pathway for L-histidine are different from each other, as shown in the attached document, Biochemical Pathways, Edited by Gerhard Michal, John

Wiley & Sons, Inc and Spektrum Akademischer Verlag Co-Publication, 1999, page 1.1. A person skilled in the art would understand that there are complicated regulation systems in the biosynthesis pathway for amino acids. Although Kino et al. disclose that the productivity of tryptophan is increased by endowing a microorganism with resistance to aminoquinoline derivative, a person skilled in the art would not, based on the disclosure of Kino and in the absence of the disclosure of the present invention, have been able to predict whether or not the productivity of histidine is increased by endowing a microorganism with resistance to aminoquinoline derivative, since regulation systems in the biosynthesis pathway is different between tryptophan and histidine. Stanbury et al. merely show a general procedure suitable to improve microbial strains for the production of amino acids. Even if Kino et al. and Stanbury et al. were combined, it would not have been obvious to a person skilled in the art that the productivity of L-histidine could be increased by providing a microorganism having an ability to produce L-histidine and having resistance to an aminoquinoline derivative.

Accordingly, it is respectfully submitted that Claims 1, 4 - 5 and 11 would not have been obvious over Kino and Stanbury, alone or in combination.

Conclusion

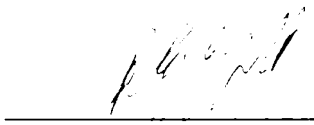
In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 1, 4, 5 and 11 are in condition for allowance. Favorable reconsideration is respectfully requested.

Should the Examiner believe that anything further is necessary to place this application in condition for allowance, the Examiner is requested to contact

applicants' undersigned attorney at the telephone number listed below.

Kindly charge any additional fees due, or credit overpayment of fees, to Deposit Account No. 01-2135 (506.39084X00).

Respectfully submitted,
ANTONELLI, TERRY, STOUT & KRAUS



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IN THE CLAIMS

1. (twice amended) A method for producing ~~an amino acid~~ L-histidine which comprises:

(a) culturing a microorganism having an ability to produce ~~an amino acid selected from the group consisting of L-alanine, L-valine, L-leucine, L-isoleucine, L-methionine, L-phenylalanine, L-proline, glycine, L-serine, L-threonine, L-cysteine, L-tyrosine, L-asparagine, L-glutamine, L-lysine,~~ L-histidine~~, L-arginine, L-aspartic acid and L-glutamic acid~~ and having resistance to 150 mg/l of an aminoquinoline derivative selected from the group consisting of chloroquine, amodiaquine, pentaquine, primaquine and the alkali metal salts of these compounds, ~~at 150 mg/l~~ in a culture medium;

(b) producing and accumulating ~~the amino acid~~ L-histidine in the culture medium; and

(c) recovering ~~the amino acid~~ L-histidine from the culture medium.

5. (amended) The method of producing ~~an amino acid~~ L-histidine according to claim 4 11, wherein the microorganism is *Escherichia coli* H-9341 (FERM BP-6674).